Specification

The Examiner requested that Applicant submit proof that pages 45-56 of the specification were part of the application as filed. The Examiner suggested that a copy of the post card submitted with the application as filed would suffice. Applicants provide a copy of pages 45-56 of the specification and a copy of the post card provided when the application was filed.

The claimed invention is supported by a specific, credible, and substantial asserted utility

The Examiner has rejected Claims 1-8 and 30-33 under 35 U.S.C. § 101, because the claimed invention allegedly is not supported by a specific, credible, and substantial asserted utility. Additionally, the Examiner has rejected Claims 1-8 and 30-33 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Applicants disagree.

Applicants have previously submitted that the claimed subject matter has utility as a diagnostic agent. For example, Applicants argued that a polynucleotide encoding a polypeptide with the amino acid sequence of SEQ ID NO 1 could be used as a diagnostic reagent to detect myocardial infarction in a subject. Accordingly, this proposed use of a polynucleotide encoding a polypeptide with the amino acid sequence of SEQ ID NO 1 as a diagnostic reagent to detect myocardial infarction in a subject is a specific, credible, and substantial utility.

The Examiner rejected this asserted utility. The Examiner reasoned that it would be necessary to obtain a tissue sample to practice a diagnostic method using the claimed subject matter. The Examiner then concluded that the requirement to obtain a tissue sample deprived the asserted utility of a "real world" application. Applicants disagree with this narrow interpretation of the utility of the claimed subject matter.

Applicants note that the claimed subject matter has utility as a diagnostic agent in a variety of embodiments. For example, the claimed polynucleotide and polypeptide encoded thereby could be used to generate diagnostic antibodies. One would expect that the polypeptide encoded by the claimed polynucleotide sequence would show elevated plasma levels as the claimed polynucleotide sequence was shown to be up-regulated in a myocardial infarction model.

The detection of increased plasma levels of the relevant protein would serve as a diagnostic marker for disease. Similar studies have been done, for example, with brain-derived natriuretic peptide (BNP), which shows elevated left verticular and left atrial gene expression in the case of certain heart diseases, as well as an increase in circulating BNP.

The generation of diagnostic antibodies is clearly disclosed in the specification. For example, as noted on page 51, lines 12-13 of the specification, the disclosed polypeptides may be used to generate antibodies. Methods for generating antibodies are discussed on pages 39-42. These antibodies in turn could be used to screen blood and other bodily fluids for the presence of a protein capable of binding to antibodies raised against the claimed subject matter. Applicants submit that the use of the claimed subject matter as a means to produce antibodies for use as a diagnostic tool is a specific, credible, and substantial utility.

Additionally, extracellular expression of the polypeptide encoded by the claimed sequence identification number is reasonably anticipated in that the sequence encodes an endogenous signal sequence as part of the primary translation product. (Specification, page 35, lines 9-12). The presence of this signal sequence as a portion of the claimed sequence provides the support necessary to support Applicants assertion that the claimed invention has a "real world" utility.

By asserting a specific, credible, and substantial utility for the claimed subject matter, (*e.g.*, use as a diagnostic agent), Applicants have satisfied the duty to assert a utility for the claimed subject matter. As such, Applicants request that the present rejection be withdrawn. Further, as Applicant has asserted a specific, credible, and substantial utility, the Section 112, first paragraph reject should also be withdrawn.

The claimed invention is supported by an adequate written description

The Examiner has rejected Claims 1, 5-8, 30, 32, and 33 under 35 U.S.C. § 112, first paragraph, as allegedly lacking an adequate written description of the claimed matter. To satisfy the written description requirement, a patent application must describe the invention in sufficient detail that one of skill in the relevant art could conclude that the inventor was in possession of the claimed invention at the time the application was filed. *See Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, (Fed. Cir. 1991). The subject matter recited in rejected Claims 1, 5-8, 30, 32, and 33 is adequately described in the specification to permit one of ordinary skill in the art to conclude Applicants were in possession of the claimed subject matter at the time the application was filed.

The Examiner has maintained the rejection of Claims 1, and 5-8 and newly rejected new Claims 30, 32, and 33 for lack of adequate written description support. The Examiner stated in the Office Action that Applicants had not demonstrated an up-regulation of the claimed sequence

in any cardiac disease model. Applicants have amended Claims 1-4, 30 and 32 to recite "a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model." By specifying a particular cardiac disease that was shown in the specification to result in the up-regulation of the claimed sequence, Applicants obviate the pending rejection. Accordingly, withdrawal of this rejection is requested.

CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 23 Dec 2002

By: _____

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IN THE CLAIMS

Please amend Claims 1-4, 30, and 32 as follows:

1. (Thrice amended) An isolated nucleic acid molecule comprising a poly- or oligonucleotide selected from the group consisting of:

(a) a polynucleotide encoding a polypeptide having at least 90% sequence identity with SEQ ID NO:1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model;

(b) a polynucleotide encoding a polypeptide having at least 90% sequence identity with amino acids 22 to 122 of SEQ ID NO:1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model;

(c) a polynucleotide encoding a polypeptide having at least 90% sequence identity with amino acids 56 to 122 of SEQ ID NO:1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model;

(d) a polynucleotide encoding amino acids 22 to 275 of SEQ ID NO:1, or a transmembrane domain deleted or inactivated variant thereof, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model;

(e) a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 22 to 122 of SEQ ID NO:1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model;

(f) a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 56 to 122 of SEQ ID NO:1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model; and

(g) the complement of a polynucleotide of (a) - (f).

2. (Twice amended) The polynucleotide of claim 1 encoding a polypeptide comprising amino acids 22 to 122 of SEQ ID NO:1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model.

3. (Twice amended) The polynucleotide of claim 1 encoding a polypeptide comprising amino acids 56 to 122 of SEQ ID NO:1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model.

4. (Twice amended) The polynucleotide of claim 1 encoding a polypeptide comprising the sequence of SEQ ID NO:1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model.

30. (Amended) An isolated polynucleotide encoding a polypeptide comprising a native mammalian homologue having at least 90% amino acid sequence identity to SEQ ID NO:1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model.

32. (Amended) An isolated polynucleotide that hybridizes to the coding region of SEQ ID NO:2 or to the complement of the coding region of SEQ ID NO:2 under stringent hybridization conditions of 50% formamide, 5x SSC, 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, 50 μg/ml salmon sperm DNA, 0.1% SDS, and 10% dextran sulfate at 42°C, and wash conditions of 0.2x SSC and 50% formamide at 55°C, followed by 0.1x SSC with EDTA at 55°C, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro myocardial infarction ~~cardiac~~ disease model.